ICU Delirium

Amra Sakusic, MD, PhD[a,b,*], Alejandro A. Rabinstein, MD[b,c]

KEYWORDS

• ICU delirium • Critical illness • Iatrogenicity
• Predisposing and precipitating risk factors

KEY POINTS

- Delirium is a common, serious, and often unrecognized complication of critical medical or surgical illnesses.
- The use of standardized validated tools for early ICU delirium detection should be incorporated into routine daily practice.
- Early detection enables timely exploration of underlying causes and facilitates appropriate management.
- Antipsychotics and sedatives should only be used for control of agitation.
- Optimizing environmental conditions, minimizing iatrogenic causes, and effectively managing the underlying illness are essential to reduce the burden of delirium in the ICU.

INTRODUCTION

Awareness of delirium in the critically ill has grown exponentially over the last couple of decades. Yet, this serious complication of critical illness remains underrecognized and insufficiently understood. In this article, we will review the definition, epidemiology, etiology and proposed pathophysiology, clinical presentation, management, and prognostic implications of delirium in the ICU.

DEFINITION

ICU Delirium encompasses a variety of symptoms that arise from generalized brain dysfunction occurring in the context of acute illness or drug intoxication. The Diagnostic and Statistical Manual of Mental Disorders (DSM-5)[1] outlines several criteria necessary for diagnosing delirium.

- Disturbance in attention and awareness that develops over a short period and represents an acute change from baseline.

[a] Neurology Department, Mayo Clinic, Jacksonville, FL, USA; [b] Neurology Department, Mayo Clinic Rochester, 200 First Street Southwest, Rochester, MN 55905, USA; [c] 1216 2nd Street Southwest, Rochester, MN 55902, USA
* Corresponding author. 200 First Street Southwest, Rochester, MN 55905.
E-mail address: sakusic.amra@mayo.edu

Neurol Clin 43 (2025) 1–13
https://doi.org/10.1016/j.ncl.2024.07.001 **neurologic.theclinics.com**
0733-8619/25/Published by Elsevier Inc.

Descargado para Anonymous User (n/a) en Autonomous University of Bucaramanga de ClinicalKey.es por Elsevier en marzo 07, 2025. Para uso personal exclusivamente. No se permiten otros usos sin autorización. Copyright ©2025. Elsevier Inc. Todos los derechos reservados.

SHOUT
SHARE
IT

- Fluctuation of attention and awareness throughout the day.
- Disturbance in cognition including impaired memory, disorientation, visual-spatial disturbance, and impairment of perception.
- Above-mentioned symptoms cannot be explained by a pre-existing neurocognitive disorder and cannot occur in the setting of a coma.
- Adequate evidence from history, physical examination, and laboratory investigations that the disturbance is a direct physiologic consequence of another medical condition, substance intoxication or withdrawal.

EPIDEMIOLOGY

Delirium is a common clinical problem. Between 10% to 16% of patients in the emergency department present with delirium,[2] while approximately 14% to 56% of hospitalized patients develop delirium at some point during hospitalization.[3] A meta-analysis of 48 studies in adult ICUs estimated a pooled prevalence of 31%,[4] but delirium has been reported to affect up to 82% of critically ill patients on mechanical ventilation.[5] Yet, the reported prevalence of delirium across different ICU cohorts has been considerably variable even among cohorts with similar measures of severity of illness. Such discrepancies signal major differences in the sensitivity of diagnosis of delirium across ICUs worldwide.

PATHOPHYSIOLOGY

The pathophysiological mechanisms underlying ICU delirium remain largely unknown. Various theories have been proposed, attributing its occurrence to impaired cerebral blood flow, neurotransmitter imbalances, genetic abnormalities, disruption of the blood-brain barrier, or exacerbated brain inflammation.[6–8] Abnormal synthesis, release, and inactivation of multiple neurotransmitters, including gamma-aminobutyric acid, acetylcholine, dopamine, and serotonin, may contribute to delirium development.[9] Meanwhile, elevated levels of proinflammatory cytokines, such as C-reactive protein and procalcitonin, that are commonly observed during acute critical illness may disrupt the blood-brain barrier, initiating a cascade of events that can precipitate delirium.[10] Cerebral metabolic failure, either by insufficient energy supply (reduced cerebral blood flow at the microcirculatory level, diminished oxygenation, relative glycopenia) or impaired energy utilization (impaired astrocyte glucose utilization), has long been reasonably suspected to play a role in the pathogenesis of ICU delirium; yet, there is scant evidence to support this theory.[11]

ETIOLOGY

The etiology of ICU delirium is multifactorial, often involving a complex interaction among various predisposing and precipitating factors. Delirium typically signifies a baseline vulnerability. Predisposing factors such as advanced age, pre-existing cognitive impairment, comorbidities, and a history of alcohol or tobacco abuse can increase a patient's susceptibility to developing delirium. Patients with extensive chronic comorbidities and reduced brain reserve may develop delirium even with a low severity of acute illness. While these factors are present upon admission and may not directly cause ICU delirium, they can make patients more prone to developing delirium when exposed to triggers such as acute illness, medications, or environmental stressors.

Precipitating factors such as mechanical ventilation, immobility, sleep disruption, urinary catheters, and multiple procedures are acquired during hospitalization. These

Descargado para Anonymous User (n/a) en Autonomous University of Bucaramanga de ClinicalKey.es por Elsevier en marzo 07, 2025. Para uso personal exclusivamente. No se permiten otros usos sin autorización. Copyright ©2025. Elsevier Inc. Todos los derechos reservados.

factors can trigger or exacerbate delirium in individuals who may already be predisposed to it. Understanding these factors and their interaction is crucial for both, the prevention and management of ICU delirium. Therefore, the individual patient's physiologic reserve and the severity of the current illness typically determine whether a patient will develop delirium during ICU hospitalization or not.

Among the numerous previously identified predisposing risk factors for delirium development, the most pertinent ones include advanced age and pre-existing cognitive dysfunction.[12–14] Indeed, more than 50% of patients who develop delirium during hospitalization have baseline cognitive impairment.[14] Additional predisposing risk factors that increase a patient's susceptibility include visual impairment, hearing loss, a history of alcohol abuse, depression, malnutrition, and baseline functional impairment.[15–17]

When assessing delirium in the ICU, it is imperative to determine the diagnosis of the acute critical illness triggering the delirium. Multiple medical conditions can be responsible for ICU delirium, including infections, metabolic derangements, autoimmune conditions, malignancies, seizures, neurodegenerative disorders, psychiatric disorders, and trauma (**Table 1**).

Furthermore, delirium may be iatrogenically caused, with polypharmacy being the most common culprit. Research indicates that the addition of three or more medications during hospitalization triples the risk of delirium.[18] While various medications can induce delirium, anticholinergic agents, opioids, benzodiazepines, and corticosteroids are most frequently implicated (see **Table 1**). Serotonin-enhancing agents and certain antibiotics (such as cefepime) can also induce delirium in susceptible patients.[19,20]

Studies specifically highlight benzodiazepines, like lorazepam and midazolam, as independent risk factors for ICU delirium, with higher doses associated with increased likelihood of occurrence.[21,22] Opioids, especially morphine, also heighten the risk of delirium, and patients receiving both opioids and benzodiazepines during their ICU stay tend to experience more prolonged delirium.[22] Delirium can also be precipitated by recreational drug use, either after intoxication or from withdrawal.

Surgical procedures have also been identified as an independent risk factor for the development of ICU delirium. Among the various surgical procedures, patients undergoing thoracic surgeries (both cardiac and non-cardiac) are particularly prone to developing ICU delirium.[23]

The ICU environment is a major sleep disruptor. Factors such as noise, constant alarms, frequent neurologic assessments, and medication administration contribute to poor sleep quality. Compromised sleep has been recognized as a risk factor for the development of delirium.[21]

CLINICAL PRESENTATION

ICU delirium can manifests in various forms, presenting a spectrum of symptoms. Critically ill patients may exhibit hypoactive, hyperactive or mixed delirium.[24]

Hypoactive delirium is characterized by reduced psychomotor activity, often resulting in patients being lethargic, withdrawn, or abulic. Conversely, hyperactive delirium manifests as agitation, combativeness, loud vocalization, aggressive behavior, hallucinations, impulsivity, and restlessness. Patients experiencing mixed hypoactive/hyperactive delirium fluctuate between the above-mentioned symptoms. In critical care settings, ICU delirium most commonly presents as hypoactive or mixed, which account for over 90% of cases. Unfortunately, hypoactive delirium is frequently overlooked and is associated with the poorest prognosis.[25]

Descargado para Anonymous User (n/a) en Autonomous University of Bucaramanga de ClinicalKey.es por Elsevier en marzo 07, 2025. Para uso personal exclusivamente. No se permiten otros usos sin autorización. Copyright ©2025. Elsevier Inc. Todos los derechos reservados.

Table 1
Causes and contributing factors of ICU delirium

Diseases	Medications	Environmental Triggers
Vascular:	Anticholinergics	Urinary catheters
• Ischemic stroke	Benzodiazepines	Restrains
• Intracranial hemorrhage	Opioids	Sleep deprivation
• Dural venous sinus thrombosis	Antihistamines	Frequent neuro checks and vital signs check
Infectious:	Antiepileptics	Constants alarms
• Meningitis/encephalitis	Muscle relaxants	Multiple procedures or surgeries
• UTI	Dopamine agonists	
• Pneumonia	Steroids	
• Intraabdominal infectious	Nonsteroidal anti-inflammatory drugs	
• Sepsis/Bacteremia	Fluoroquinolones	
• Endocarditis	Cephalosporins	
Autoimmune:	Beta blockers	
• Autoimmune encephalitis	Digitalis	
• Neuropsychiatric lupus	Lithium	
Metabolic:	Monoamine oxidase inhibitor	
• Electrolyte disarrangements		
• Hepatic encephalopathy		
• Uremic encephalopathy		
• Hypoxia		
• Hypercarbia		
• Dehydration		
• Nutritional deficiencies		
Endocrine:		
• Hypothyroidism		
• Hyperthyroidism		
• Hypoglycemia		
• Hyperglycemia		
• Hypercortisolism		
• Hypocortisolism		
Neoplasm:		
• Primary CNS tumor		
• Brain metastasis		
• Carcinomatous meningitis		
• Paraneoplastic encephalitis		
Epilepsy:		
• Seizures		
• Non-convulsive status epilepticus		
Psychiatric disorders		
Neuroleptic malignant syndrome		
Serotonin syndrome		
Other toxidromes		

DIAGNOSIS

To ensure delirium is not missed and is timely managed upon recognition, utilizing validated standardized tools for ICU delirium detection is crucial. Routine implementation of the Confusion Assessment Method for the ICU (CAM-ICU) score (Fig. 1) for every patient in the ICU, except those with a Richmond Agitation Sedation Scale score less than −3 (ie, deeply sedated) (Table 2), has been shown to reduce unrecognized cases.[26] However, systematic screening for delirium remains deficient in many ICUs. Nurses frequently find diagnosing delirium in intubated and sedated patients challenging, although the CAM-ICU score is specifically tailored for this population.

Descargado para Anonymous User (n/a) en Autonomous University of Bucaramanga de ClinicalKey.es por Elsevier en marzo 07, 2025. Para uso personal exclusivamente. No se permiten otros usos sin autorización. Copyright ©2025. Elsevier Inc. Todos los derechos reservados.

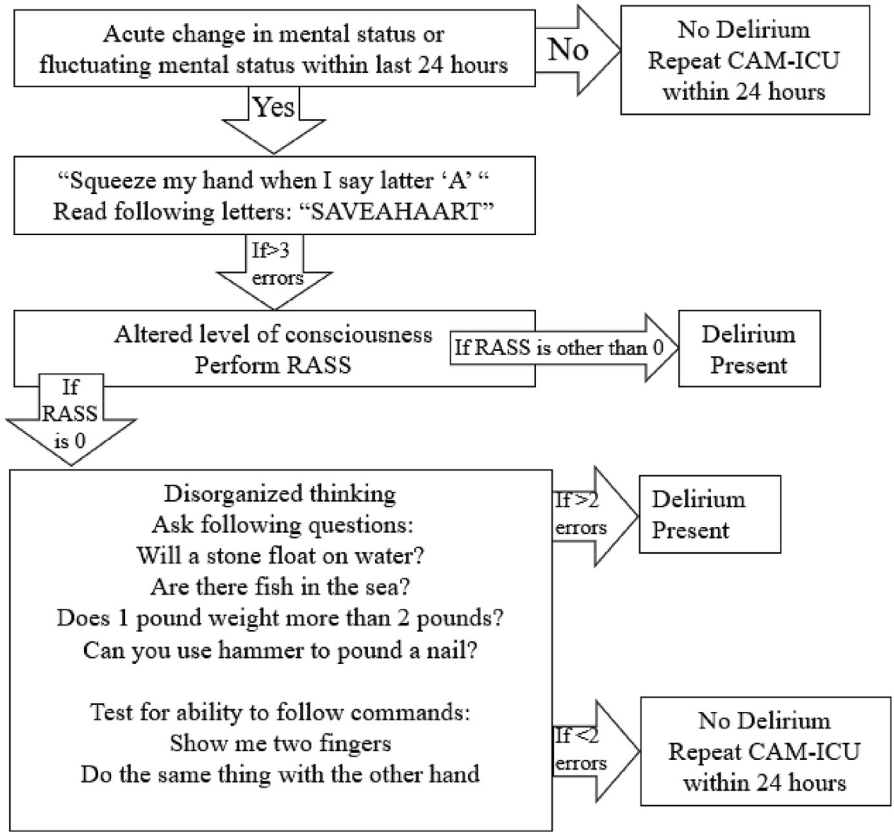
Acute change in mental status or fluctuating mental status within last 24 hours
No
No Delirium Repeat CAM-ICU within 24 hours
Yes
"Squeeze my hand when I say latter 'A' " Read following letters: "SAVEAHAART"
If>3 errors
Altered level of consciousness Perform RASS
If RASS is other than 0
Delirium Present
If RASS is 0
Disorganized thinking
Ask following questions:
Will a stone float on water?
Are there fish in the sea?
Does 1 pound weight more than 2 pounds?
Can you use hammer to pound a nail?
Test for ability to follow commands:
Show me two fingers
Do the same thing with the other hand
If >2 errors
Delirium Present
If <2 errors
No Delirium Repeat CAM-ICU within 24 hours

Fig. 1. Confusion assessment method in the ICU-CAM-ICU.

Despite concerns about its perceived time-consuming nature and complexity,[27] studies indicate that completing the CAM-ICU assessment typically takes only 2 to 5 minutes.[28] The Intensive Care Delirium Screening Checklist (ICDSC) is another useful tool for the bedside detection of delirium.[29] Unlike the CAM-ICU (a dichotomous

Table 2
Richmond agitation sedation scale for the assessment of depth of sedation

+4	Very combative, violent, dangers to staff
+3	Pulling catheters and tubes, aggressive
+2	Frequent non purposeful movements, fights ventilator
+1	Anxious but movements not aggressive or vigorous
0	Alert and calm
−1	Awakes (eye contact) for > 10 s in response to voice
−2	Awakes (eye contact) for < 10 s in response to voice
−3	Eye opening or movement to voice without eyes contact
−4	No response to voice, but eye opening or movement to physical stimulation
−5	No response to voice or physical stimulation

Descargado para Anonymous User (n/a) en Autonomous University of Bucaramanga de ClinicalKey.es por Elsevier en marzo 07, 2025. Para uso personal exclusivamente. No se permiten otros usos sin autorización. Copyright ©2025. Elsevier Inc. Todos los derechos reservados.

score), the ICDSC (an ordinal scale) can gauge delirium severity. The CAM-ICU-7 is a modification of the CAM-ICU designed to provide information on delirium severity.[30] Good correlation between the ICDSC and CAM-ICU-7 has been reported.[31]

It is well-established that without the use of standardized validated tools, delirium in the ICU often goes unnoticed, therefore, we strongly advocate for daily screening (ideally once every nursing shift) using validated tools, as missed diagnoses can lead to lack of appropriate treatment.

TREATMENT

Medical/Pharmacologic Management

Managing ICU delirium has always posed challenges due to limited pharmacologic options. Historically, haloperidol was the preferred agent, based on a small study involving 15 delirious ICU patients who underwent cardiac surgery in 1978.[32] In 2002, SCCM guidelines also recommended haloperidol for managing ICU delirium. However, this recommendation was reconsidered when subsequent studies revealed that first-generation antipsychotics increase mortality rates among elderly patients.[33]

Perspectives on antipsychotic use shifted after a randomized controlled trial involving 142 mechanically ventilated patients with delirium. Patients were randomized to receive either intravenous haloperidol or normal saline until delirium-free or discharged from the ICU. The study found no difference in delirium-free days, delirium duration, or survival between the groups.[34]

Similarly, the MIND USA trial, a randomized double-blind controlled trial comparing ziprasidone, haloperidol, and placebo, found no difference in delirium-free days or survival among patients receiving antipsychotics versus placebo. Interestingly, a randomized double-blind study among hospice patients comparing haloperidol, risperidone, and placebo found an increase in delirium symptom severity among those who received antipsychotics.[35]

These studies led to a change in SCCM guidelines, advising against the routine use of haloperidol or atypical antipsychotics for delirium treatment in critically ill patients.[36]

The use of pharmacologic agents like dexmedetomidine and ketamine remains a subject of debate. Double-blind randomized controlled trials comparing dexmedetomidine to midazolam or lorazepam revealed that patients sedated with dexmedetomidine had a 23% lower risk of delirium compared to those treated with midazolam[37] and experienced half as many delirium days compared to patients treated with lorazepam.[38] A recent Cochrane analysis suggested that dexmedetomidine may shorten delirium duration, mechanical ventilation, and ICU stay, with no reported difference in long-term cognitive impairment or mortality.[39]

Moreover, a randomized controlled trial comparing a single intraoperative dose of ketamine to placebo found no difference in delirium incidence between the groups, although patients in the ketamine group experienced a higher incidence of hallucinations and nightmares.[40]

To date, no pharmacologic agent has demonstrated a significant effect on delirium incidence, duration, or prevention. Therefore, current SCCM guidelines advise against the routine use of dexmedetomidine, ketamine, or first- or second-generation antipsychotics in delirium management.[36] However, if we need to treat agitated delirious patient to prevent injury from agitation, dexmedetomidine may be a preferred agent.

NONPHARMACOLOGICAL MANAGEMENT

Prevention strategies, such as limiting risk factors, promoting optimal sleep hygiene, employing a judicious approach to analgosedation, avoiding unnecessary invasive

Descargado para Anonymous User (n/a) en Autonomous University of Bucaramanga de ClinicalKey.es por Elsevier en marzo 07, 2025. Para uso personal exclusivamente. No se permiten otros usos sin autorización. Copyright ©2025. Elsevier Inc. Todos los derechos reservados.

procedures, facilitating early mobilization, and providing frequent reorientation, have become the cornerstone of delirium management in the ICU.

ABCDEF bundle (Fig. 2) is a validated comprehensive approach to managing critically ill patients in the ICU, with a specific focus on preventing and managing delirium.[41] Each letter in the ABCDEF bundle represents a different component of care aimed at optimizing the quality of ICU care: assessment of pain, effective delivery of analgesia and judicious use of sedation, daily spontaneous awakening trials (when appropriate coupled with spontaneous breathing trials), delirium monitoring/management, early

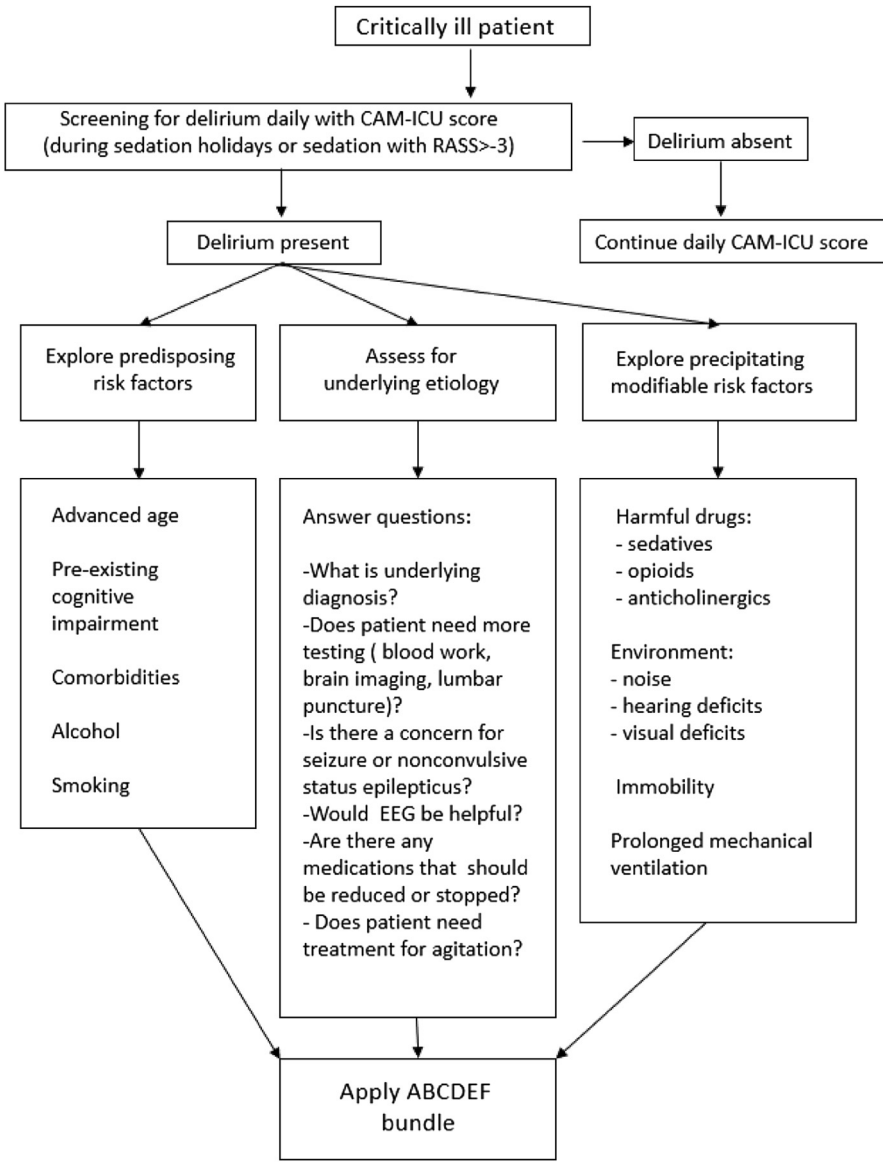

Fig. 2. Approach to ICU delirium.

Descargado para Anonymous User (n/a) en Autonomous University of Bucaramanga de ClinicalKey.es por Elsevier en marzo 07, 2025. Para uso personal exclusivamente. No se permiten otros usos sin autorización. Copyright ©2025. Elsevier Inc. Todos los derechos reservados.

exercise/mobility, and family engagement and empowerment. By addressing these six key components of care, the ABCDEF bundle may improve patient-centered outcomes, including a reduction in the incidence of delirium. Implementing the ABCDEF bundle requires a multidisciplinary team approach involving physicians, nurses, physical therapists, respiratory therapists, pharmacists, and other healthcare providers. There is evidence that compliance with the ABCDEF bundle is associated with a reduction in mortality and an increased number of delirium-free days,[42] though the beneficial impact of the bundle on the occurrence and duration of delirium has not fully consistent across different studies.[43]

PROGNOSTIC IMPLICATIONS

Delirium is associated with poor outcomes and increased mortality both during hospitalization and up to 1 year after discharge.[44,45] Patients who develop delirium within the first 24 hours of ICU admission have a higher risk of in-hospital mortality.[46] Delirious patients often require prolonged mechanical ventilation and face challenges during the weaning process.[47–49] In addition to having worse short-term outcomes, patients who experience delirium during hospitalization are at increased risk of developing dementia within the subsequent year, compared to those without delirium.[50,51]

Research indicates that over 70% of ICU survivors who experienced delirium during hospitalization exhibit cognitive impairment at 3- and 12-month follow-up, with a significant proportion experiencing moderate to severe impairment.[27,28,52] Notably, patients with pre-existing Alzheimer disease who develop delirium during ICU admission experience a worse trajectory of cognitive decline compared to those without delirium, even after accounting for disease severity and comorbidities. Neuroimaging in these patients confirms greater brain atrophy and more severe white matter disease.[53]

Delirium is often dismissed as a transient and benign condition, particularly among older patients, but this is a hazardous misconception. Delirious patients older than 65 years have a twofold increased mortality rate as compared to those who do not develop delirium during hospitalization.[51] Therefore, early recognition, prevention, and management of delirium must be a priority when caring for older critically ill patients.

The socioeconomic burden of delirium is substantial. Occurrence of delirium is associated with longer ICU and hospital stays, increased likelihood of discharge to skilled nursing facilities, and higher healthcare costs.[54–57] Delirious patients are less likely to return to work after discharge compared to those without delirium during hospitalization.[58]

Lastly, the psychological impact of delirium on ICU patients is substantial, with over 30% of survivors reporting depressive symptoms at 3-month follow-up, and 7% receiving a diagnosis of posttraumatic stress disorder (PTSD). Pre-existing diagnoses of military-associated PTSD, anxiety, and depression are associated with a higher likelihood of developing ICU-related PTSD[59,60]

SUMMARY: WHAT TO REMEMBER AT THE BEDSIDE

ICU delirium is a prevalent and severe complication of critical illness, associated with increased morbidity, prolonged mechanical ventilation, extended hospital stays, exacerbated cognitive decline, and higher mortality rates. Despite increased awareness of the problem by ICU providers, delirium still often goes undetected and underdiagnosed. It is crucial to remember that most cases of delirium are hypoactive. While hyperactive delirium is more obvious, hypoactive delirium may carry worse prognosis.

Descargado para Anonymous User (n/a) en Autonomous University of Bucaramanga de ClinicalKey.es por Elsevier en marzo 07, 2025. Para uso personal exclusivamente. No se permiten otros usos sin autorización. Copyright ©2025. Elsevier Inc. Todos los derechos reservados.

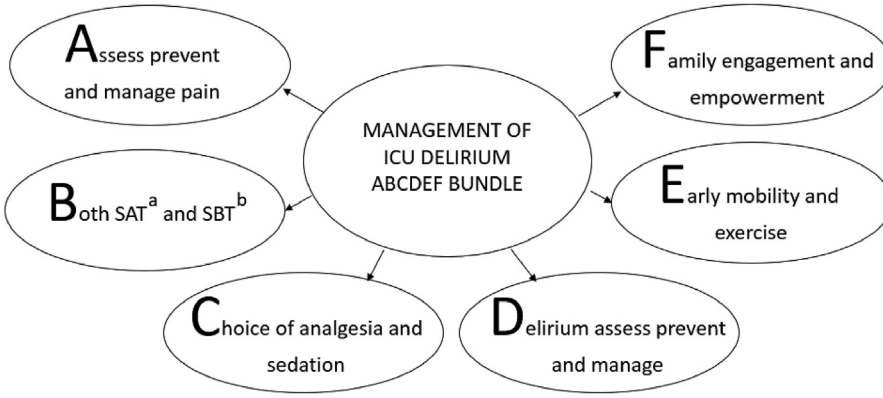
Assess prevent and manage pain
Family engagement and empowerment
MANAGEMENT OF ICU DELIRIUM ABCDEF BUNDLE
Both SAT[a] and SBT[b]
Early mobility and exercise
Choice of analgesia and sedation
Delirium assess prevent and manage

Fig. 3. ABCDEF bundle. SAT, spontaneous awakening trials; SBT, spontaneous breathing trials.

Upon detecting delirium, physicians must investigate its underlying etiology. Key questions to address include determining if the underlying diagnosis is known; whether additional testing is necessary (such as blood work, brain imaging, electroencephalography or lumbar puncture); evaluating potentially harmful medications that should be reduced or discontinued; identifying factors that could exacerbate delirium (such as removable indwelling catheters, sleep deprivation, poor mobilization, or missing hearing aids or glasses); and assessing the need for agitation treatment (see **Fig. 2**). Once these questions are addressed, a multidisciplinary ICU team including physicians, nurses, physical therapists and respiratory therapists should implement the ABCDEF bundle (**Fig. 3**). Simple non-pharmacological interventions incorporated into this bundle - such as frequent reorientation, ensuring good quality of sleep, and providing hearing aids or glasses - can be useful to reduce the burden of delirium. Minimizing sedation, particularly with benzodiazepines, may help avert or mitigate delirium. Antipsychotic medications (eg, haloperidol, quetiapine or olanzapine) should be reserved for patients with overt agitation, understanding that they do not treat the delirium per se or reduce its duration.

ICU delirium is far from benign and is linked to serious complications. Unfortunately, it is often overlooked, highlighting the need for increased attention to its detection, management, and prevention. Regular utilization of validated tools for early detection, such as the CAM-ICU score, is strongly advised. It's important for clinicians to recognize that agitation may not always be present and that hypoactive delirium, while more common, poses a greater diagnostic challenge and carries a poorer prognosis. Understanding the underlying causes is essential for effective management.

CLINICS CARE POINTS

- Think about ICU delirium in your everyday practice
- Utilize standardized and validated tools for early delirium detection
- Investigate potential causes and eliminate iatrogenic factors
- Address the underlying critical illness
- Reduce environmental factors that may exacerbate delirium

Descargado para Anonymous User (n/a) en Autonomous University of Bucaramanga de ClinicalKey.es por Elsevier en marzo 07, 2025. Para uso personal exclusivamente. No se permiten otros usos sin autorización. Copyright ©2025. Elsevier Inc. Todos los derechos reservados.

- Encourage early mobilization
- Prioritize quality of sleep
- Limit the use of sedatives, antipsychotics, and opioids whenever feasible.
- Implement the ABCDF bundle
- Engage multidisciplinary teams for comprehensive care

DISCLOSURE

Authors declare that they have no conflict of interest.

REFERENCES

1. American Psychiatric Association. Diagnostic and statistical manual of mental disorders: DSM-5. Washington, DC: American Psychiatric Association; 2013.
2. Hustey FM, Meldon SW. The prevalence and documentation of impaired mental status in elderly emergency department patients. Ann Emerg Med 2002;39(3): 248–53.
3. Siddiqi N, Stockdale R, Britton AM, et al. Interventions for preventing delirium in hospitalized patients. Cochrane Database Syst Rev 2007;(2):CD005563.
4. Krewulak KD, Stelfox HT, Leigh JP, et al. Incidence and prevalence of delirium subtypes in an adult ICU: a systematic review and meta-analysis. Crit Care Med 2018 Dec;46(12):2029–35.
5. Ely EW, Shintani A, Truman B, et al. Delirium as a predictor of mortality in mechanically ventilated patients in the intensive care unit. JAMA 2004;291(14):1753–62.
6. van Gool WA, van de Beek D, Eikelenboom P. Systemic infection and delirium: when cytokines and acetylcholine collide. Lancet 2010;375(9716):773–5, 17.
7. Inouye SK, Ferrucci L. Elucidating the pathophysiology of delirium and the interrelationship of delirium and dementia. J Gerontol A Biol Sci Med Sci 2006;61(12): 1277–80.
8. Inouye SK, Westendorp RG, Saczynski JS. Delirium in elderly people. Lancet 2014;383(9920):911–22.
9. Figueroa-Ramos MI, Arroyo-Novoa CM, Lee KA, et al. Sleep and delirium in ICU patients: a review of mechanisms and manifestations. Intensive Care Med 2009; 35(05):781–95.
10. Ali S, Patel M, Jabeen S, et al. Insight into delirium. Innov Clin Neurosci 2011; 8(10):25–34.
11. Wilson JE, Mart MF, Cunningham C, et al. Delirium. Nat Rev Dis Prim 2020 Nov 12;6(1):90.
12. Francis J, Martin D, Kapoor WN. A prospective study of delirium in hospitalized elderly. JAMA 1990;263(8):1097–101.
13. Inouye SK, Charpentier PA. Precipitating factors for delirium in hospitalized elderly persons: predictive model and interrelationship with baseline vulnerability. JAMA 1996;275(11):852–7.
14. McNicoll L, Pisani MA, Zhang Y, et al. Delirium in the intensive care unit: occurrence and clinical course in older patients. J Am Geriatr Soc 2003;51(5):591–8.
15. Van Rompaey B, Elseviers MM, Schuurmans MJ, et al. Risk factors for delirium in intensive care patients: a prospective cohort study. Crit Care 2009;13(03):R77.
16. Ouimet S, Kavanagh BP, Gottfried SB, et al. Incidence, risk factors and consequences of ICU delirium. Intensive Care Med 2007;33(01):66–73.

Descargado para Anonymous User (n/a) en Autonomous University of Bucaramanga de ClinicalKey.es por Elsevier en marzo 07, 2025. Para uso personal exclusivamente. No se permiten otros usos sin autorización. Copyright ©2025. Elsevier Inc. Todos los derechos reservados.

17. Santos FS, Velasco IT, Fráguas R Jr. Risk factors for delirium in the elderly after coronary artery bypass graft surgery. Int Psychogeriatr 2004;16(02):175–93.
18. Inouye SK, Rushing JT, Foreman MD, et al. Does delirium contribute to poor hospital outcomes?: a three-site epidemiologic study. J Gen Intern Med 1998;13(4):234–42.
19. Pedavally S, Fugate JE, Rabinstein AA. Serotonin syndrome in the intensive care unit: clinical presentations and precipitating medications. Neurocritical Care 2014;21(1):108–13.
20. Singh TD, O'Horo JC, Day CN, et al. Cefepime is Associated with Acute Encephalopathy in Critically Ill Patients: A Retrospective Case-Control Study 2020;33(3):695–700.
21. Ramos MF, Arroyo-Novoa CM, Lee KA, et al. Sleep and delirium in ICU patients: a review of mechanisms and manifestations. Intensive Care Med 2009;35(5):781–95.
22. Pisani MA, Murphy TE, Araujo KL, et al. Benzodiazepine and opioid use and the duration of intensive care unit delirium in an older population. Crit Care Med 2009;37(01):177–83.
23. Douglas VC, Josephson SA. Delirium. Continuum Lifelong Learning Neurol 2010;16(2).
24. Wijdicks EFM, Rabinstein AA. What is it like to be delirious? Neurocritical Care 2022;37(1):1–5.
25. Peterson JF, Pun BT, Dittus RS, et al. Delirium and its motoric subtypes: a study of 614 critically ill patients. J Am Geriatr Soc 2006;54(03):479–84.
26. Ely EW, Inouye SK, Bernard GR, et al. Delirium in mechanically ventilated patients: validity and reliability of the confusion assessment method for the intensive care unit (CAM-ICU). JAMA 2001;286(21):2703–10.
27. Devlin JW, Fong JJ, Howard EP, et al. Assessment of delirium in the intensive care unit: nursing practices and perceptions. Am J Crit Care 2008;17(06):555–65.
28. Andrews L, Silva SG, Kaplan S, et al. Delirium monitoring and patient outcomes in a general intensive care unit. American journal of critical care: an official publication. Am J Crit Care 2015;24:48–56.
29. Bergeron N, Dubois MJ, Dumont M, et al. Intensive care delirium screening checklist: evaluation of a new screening tool. Intensive Care Med 2001;27(5):859–64.
30. Khan BA, Perkins AJ, Gao S, et al. The confusion assessment method for the ICU-7 delirium severity scale: a novel delirium severity instrument for use in the ICU. Crit Care Med 2017;45(5):851–7.
31. Krewulak KD, Rosgen BK, Ely EW, et al. The CAM-ICU-7 and ICDSC as measures of delirium severity in critically ill adult patients. PLoS One 2020;15(11):e0242378.
32. Cassem N. Intravenous use of haloperidol for acute delirium in intensive care settings. In: Continuing Medical education syllabus and scientific proceedings in summary form from the 131st Annual Meeting of the394. Washington, DC: American Psychiatric Association; 1978. p. 204–5.
33. Jacobi J, Fraser GL, Coursin DB, et al, Task Force of the American College of Critical Care Medicine (ACCM) of the Society of Critical Care Medicine (SCCM), American Society of Health-System Pharmacists (ASHP), American College of Chest Physicians. Clinical practice guidelines for the sustained use of sedatives and analgesics in the critically ill adult. Crit Care Med 2002;30(01):119–41.
34. Page VJ, Ely EW, Gates S, et al. Effect of intravenous haloperidol on the duration of delirium and coma in critically ill patients (Hope-ICU): a randomised, double-blind, placebo-controlled trial. Lancet Respir Med 2013;1(07):515–23.

Descargado para Anonymous User (n/a) en Autonomous University of Bucaramanga de ClinicalKey.es por Elsevier en marzo 07, 2025. Para uso personal exclusivamente. No se permiten otros usos sin autorización. Copyright ©2025. Elsevier Inc. Todos los derechos reservados.

35. Agar MR, Lawlor PG, Quinn S, et al. Efficacy of oral risperidone, haloperidol, or placebo for symptoms of delirium among patients in palliative care: a randomized clinical trial. JAMA Intern Med 2017;177(01):34–42.
36. Devlin JW, Skrobik Y, Gélinas C, et al. Clinical practice guidelines for the prevention and management of pain, agitation/sedation, delirium, immobility, and sleep disruption in adult patients in the ICU. Crit Care Med 2018;46(09):e825–73.
37. Riker RR, Shehabi Y, Bokesch PM, et al, SEDCOM (Safety and Efficacy of Dexmedetomidine Compared With Midazolam) Study Group. Dexmedetomidine vs midazolam for sedation of critically ill patients: a randomized trial. JAMA 2009; 301(05):489–99.
38. Pandharipande PP, Pun BT, Herr DL, et al. Effect of sedation with dexmedetomidine vs lorazepam on acute brain dysfunction in mechanically ventilated patients: the MENDS randomized controlled trial. JAMA 2007;298(22):2644–53.
39. Burry L, Hutton B, Williamson DR, et al. Pharmacological interventions for the treatment of delirium in critically ill adults. Cochrane Database Syst Rev 2019; 9:CD011749.
40. Avidan MS, Maybrier HR, Abdallah AB, et al, PODCAST Research Group. Intraoperative ketamine for prevention of postoperative delirium or pain after major surgery in older adults: an international, multicentre, double-blind, randomised clinical trial. Lancet 2017;390(10091):267–75.
41. Ely EW. The ABCDEF bundle: science and philosophy of how ICU liberation serves patients and families. Crit Care Med 2017;45(2):321–30.
42. Pun BT, Balas MC, Barnes-Daly MA, et al. Caring for critically ill patients with the ABCDEF bundle: results of the ICU liberation collaborative in over 15,000 adults. Crit Care Med 2019;47(01):3–14.
43. Zhang S, Han Y, Xiao Q, et al. Effectiveness of bundle interventions on ICU delirium: a meta-analysis. Crit Care Med 2021;49(2):335–46.
44. Siddiqi N, House AO, Holmes JD. Occurrence and outcome of delirium in medical in-patients: a systematic literature review. Age Ageing 2006;35(04):350–64, 32.
45. Witlox J, Eurelings LS, de Jonghe JF, et al. Delirium in elderly patients and the risk of post-discharge mortality, institutionalization, and dementia: a meta-analysis. JAMA 2010;304(04):443–51.
46. van den Boogaard M, Peters SAE, van der Hoeven JG, et al. The impact of delirium on the prediction of in-hospital mortality in intensive care patients. Crit Care 2010;14(04):R146.
47. Zhang Z, Pan L, Ni H. Impact of delirium on clinical outcome in critically ill patients: a meta-analysis. Gen Hosp Psychiatr 2013;35(02):105–11.
48. Salluh JI, Wang H, Schneider EB, et al. Outcome of delirium in critically ill patients: systematic review and meta-analysis. BMJ 2015;350:h2538.
49. Dessap AM, Roche-Campo F, Launay J-M, et al. Delirium and circadian rhythm of melatonin during weaning from mechanical ventilation: an ancillary study of a weaning trial. Chest 2015;148(05):1231–41.
50. McCusker J, Cole M, Dendukuri N, et al. Delirium in older medical inpatients and subsequent cognitive and functional status: a prospective study. CMAJ (Can Med Assoc J) 2001;165(5):575–83.
51. Rockwood K, Cosway S, Carver D, et al. The risk of dementia and death after delirium. Age Ageing 1999;28(6):551–6.
52. Sakusic A, Gajic O, Singh TD, et al. Risk factors for persistent cognitive impairment after critical illness, nested case-control study. Crit Care Med 2018;46(12):1977–84.
53. Gross AL, Jones RN, Habtemariam DA, et al. Delirium and long-term cognitive trajectory among persons with dementia. Arch Intern Med 2012;172(17):1324–31.

Descargado para Anonymous User (n/a) en Autonomous University of Bucaramanga de ClinicalKey.es por Elsevier en marzo 07, 2025. Para uso personal exclusivamente. No se permiten otros usos sin autorización. Copyright ©2025. Elsevier Inc. Todos los derechos reservados.

54. Ely EW, Gautam S, Margolin R, et al. The impact of delirium in the intensive care unit on hospital length of stay. Intensive Care Med 2001;27(12):1892–900.
55. Thomason JW, Shintani A, Peterson JF, et al. Intensive care unit delirium is an independent predictor of longer hospital stay: a prospective analysis of 261 non-ventilated patients. Crit Care 2005;9(04):R375–81.
56. Milbrandt EB, Deppen S, Harrison PL, et al. Costs associated with delirium in mechanically ventilated patients. Crit Care Med 2004;32(04):955–62.
57. Leslie DL, Marcantonio ER, Zhang Y, et al. One-year health care costs associated with delirium in the elderly population. Arch Intern Med 2008;168(01):27–32.
58. Norman B, Jackson J, Graves J, et al. Employment changes after critical illness. Am J Respir Crit Care Med 2014;44(11):2003–9.
59. Jackson JC, Pandharipande PP, Girard TD, et al. Bringing to light the Risk Factors And Incidence of Neuropsychological dysfunction in ICU survivors (BRAIN-ICU) study investigators. Depression, post-traumatic stress disorder, and functional disability in survivors of critical illness in the BRAIN-ICU study: a longitudinal cohort study. Lancet Respir Med 2014;2(05):369–79.
60. Patel MB, Jackson JC, Morandi A, et al. Incidence and risk factors for intensive care unit-related post-traumatic stress disorder in veterans and civilians. Am J Respir Crit Care Med 2016;193(12):1373–81.

Descargado para Anonymous User (n/a) en Autonomous University of Bucaramanga de ClinicalKey.es por Elsevier en marzo 07, 2025. Para uso personal exclusivamente. No se permiten otros usos sin autorización. Copyright ©2025. Elsevier Inc. Todos los derechos reservados.